REMARKS/ARGUMENTS

By the present amendment, claims 1, 5-12, 14-58, and 62-63 are pending in this application. Claims 2-4, 13, and 59-61 were previously canceled without prejudice. Claims 1 and 42 are amended herein to more particularly define the invention and to claim it with greater specificity. Claims 62 and 63 are added herein. The subject matter recited in these claims is directed to three specific therapeutic complexes and a list of disorders. Basis for these amendments and newly added claims may be found throughout the specification and claims as originally filed. No new matter have been added.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

Written Description

Claims 1, 5-12, and 14-58

Claims 1, 5-12, and 14-58 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention (the written description requirement) (items 3 and 4 on pages 2 and 5 of the Office Action). In particular, the Examiner has stated that the limitation "R_3 is a phosphate or phosphonate derivative of a therapeutically active agent" is allegedly not disclosed in the specification, and thus presents a new matter.

The rejections is respectfully traversed. The Applicants respectfully disagree that the limitation defining the substitutent R_3 constitutes new matter. The Applicants would like to direct the Examiner's attention to the disclosure provided in paragraphs [0034]-[0036] on pages 7-8 of the original application, showing the R_3 group attached to the rest of the molecule. The Applicants further point out that the original Figures 1a and 1b clearly show that "R_3 is a phosphate or phosphonate derivative of a therapeutically active

agent." The same is additionally disclosed in paragraphs [0026], [0051], and [0078] on pages 5, 12, and 22, respectively, of the original application. Accordingly, it is submitted that the limitation "R_3 is a phosphate or phosphonate derivative of a therapeutically active agent" is adequately disclosed in the original specification, and, therefore, does not constitute a new matter.

Claims 1, 27, and 42

In addition, claims 1, 27, and 42 stand further rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention (the written description requirement) (item 5 on pages 5 of the Office Action).

In particular, the Examiner has stated that only a limited number of substituents R_1, R_1', R_2, and R_2' has been exemplified and that the number of examples does not justify the breadth of claims as recited because it does not sufficiently demonstrate possession of all the species claimed.

The Applicants respectfully disagree with this characterization. The burden of showing the insufficiency of written description is squarely the Examiner's, as required by *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1 976). MPEP specifically states that a strong presumption of adequacy of written description exists and directs that § 112, paragraph 1 rejections of an original claim should be rare. MPEP §§2163(I)(A) and 2163(II)(A). It is respectfully submitted that in this case the Examiner has not met the burden of demonstrating an alleged lack of written description.

The legal standard for determining the adequacy of written description is clear and well established. The description is adequate if "the disclosure of the application relied upon reasonably conveys to the artisan that the inventor had possession at [the time of filing] of the later claimed subject matter." *Wang Labs Inc. v. Toshiba Corp.*, 993 F.2d

858, 26 USPQ2d 1767. In other words, the question of the lack of adequate written description does not arise unless "one skilled in the art [would not be able] to immediately envisage the product claimed..." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 39 USPQ2d 1895. It is submitted that applying these broad principles to the pending claims, it can be unequivocally concluded that the written description in this application adequately supports the claims.

The current test for sufficiency of written description is whether a description of the invention is such that it allows those of skill in the art to distinguish the subject matter claimed and at issue, from other related subject matter. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). Accordingly, to satisfy the written description requirement, a claim directed to a genus has to be supported by a sufficient description of a representative number of species. *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The requirement of providing a "description of a representative number of species" was interpreted in the *Enzo* case by holding that to comply with the written description requirement, a claim directed to a genus must be supported by a description that "indicates that the patentee has invented species sufficient to constitute the genus." *Enzo*, 296 F.3d at 966, 63 USPQ2d at 1615.

It is respectfully submitted that the test of sufficiency of written description has been satisfied in this case. Indeed, a number of particular species that may be used have been provided. These species include products based on ethanediol, propanediol, or butanediol (paragraph [0034] on page 7 of the specification), and further details are provided as to the compounds that may be used (paragraphs [0034]-[0036] on pages 7-8 of the specification). Furthermore, a number of exemplary nucleosides, therapeutically active agents, among others, that can be used in the complexes are provided (e.g., paragraphs [0037]-[0040] on pages 8-9 of the specification). Finally, a number of particular compounds, such as HDP-P-Aga-G, HDP-cCDV, or HDP-P-GCV are also

provided (e.g., paragraphs [0035] and [0066] on pages 8 and 15 of the specification for HDP-P-Aga-G and HDP-P-GCV, and Figure 1a for HDP-cCDV).

It is, therefore, submitted that the application provides a sufficient description of a representative number of species to be able to provide support for the entire genus, and that the possession has been clearly shown.

Enablement

Claims 1, 5-12, and 14-58

Claims 1, 5-12, and 14-58 stand further rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement (item 6 on page 7 of the Office Action). The Examiner has stated that the specification only contained a few examples, and there will be required too much experimentation to provide the requisite enablement to all the complexes. In other words, in the Examiner's opinion, the claims are too broad (see, page 6, second paragraph of the Office Action).

The rejection is respectfully traversed on the ground that the Examiner has not met the burden of demonstrating that the entire breadth and scope of the claims is allegedly not enabled.

Just as for the written description-based rejections, the burden of demonstrating that the claims are not properly enabled is squarely on the Examiner, as required by *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). It is settled law that a presumption of enablement exists, and that ordinarily the lack of enablement rejection should not be given unless there are reasons to doubt the veracity of the statements in the application upon which the reliance for enablement is based. MPEP § 2164.04. It is respectfully submitted that in this case the Examiner has not met the burden of demonstrating the alleged lack of enablement.

The legal standard for determining the adequacy of enablement is well established. To be enabling, "the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *Genentech Inc. v. NovoNordisk*, 108 F.3d 1361, 42 USPQ2d 1001 (Fed. Cir. 1997). Indeed, it is well established that as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied. *In re Fisher* , 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The Applicants submit that the specification does comply with the enablement requirement.

The Examiner's rationale for making this rejection is based on the assertion that too much experimentation would be needed to practice the invention, in view of the specific experimental results that have been provided in the specification (see, item 7 on page 8 of the specification). The Applicants disagree.

Indeed, the specification teaches using the compounds recited in claim 1 for treating pathological condition of ocular tissue, where the conditions being treated are limited just to macular degeneration, eye trauma, a pre-existing retinal detachment, ocular proliferative or vascular diseases, or diseases of elevated intraocular pressure. It is clear from the specification that compounds shown in claim 1 are capable of achieving good results when used for such treatments. The unambiguous teaching of that may be found in many passages throughout the specification. See, e.g., paragraph [0024] on page 5 (ocular treatments), paragraph [0027] bridging pages 5 and 6 (compounds to be used), paragraphs [0057], [0075], [0053], and [0078] on pages 13, 20, 12, and 22, respectively (more specific eye disorders). As discussed above, some specific compounds to be used are explicitly named (i.e., HDP-P-Aga-G, HDP-cCDV, or HDP-P-GCV). Furthermore, the specification provides clear guidelines and teaching as to the treatment regimen, including the dosages, methods of application and the like. See, e.g., paragraphs [0052]. [0060], and [0061] on pages 12 and 14.

Accordingly, the specification clearly identifies the types of eye disorders to which the treatments that are described are applicable, and the compounds that may be used for such treatments. Based on what is actually specifically described and taught, those having ordinary skill in the art would be able to make a simple extrapolations and would know what compounds are to be used for the treatment of which eye disorders.

While it's true that the specification does not discuss or exemplify every possible treatment or compound, it is never required. As provided by the case law, providing just one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim is enough. See, *In re Fisher*, *supra*. And it is exceedingly clear that the application teaches and enables more than just one specific embodiment of the invention. The Examiner himself has identified at least a few such specific examples of enabled treatments.

Accordingly, it is the Applicants' position that the specification clearly teaches methods bearing good correlation to the entire scope of all the claims, indicating that the test of enablement has been met.

Finally, the Applicants respectfully point out that it is only the necessity of undue experimentation that may make a specification non-enabling. Modest, reasonable quantity of experimentation is allowed, if it is routine or if the specification provides enough guidance. *In re Wands* , 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). It has never been the rule that the specification itself must necessarily describe how to use every possible variant of the claimed invention. Indeed, "the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003).

Applying these principles to the facts of the present case, it is clear that the specification describes specific examples of ocular treatments, however, in practicing the invention with respect to all kinds of eye disorders, the principles and basic methodology

will remain the same. The specification makes it clear that the unique properties of the compounds of the genus identified in claim 1 allow these compounds to serve as effective treatment agents. Once such compounds are identified (such as compounds specifically exemplified), the rest is a matter of routine experimentation. Some adjustment may be needed in view of a possibility of some differences in activities. It is the Applicants' position that making such adjustments would require performing not more than common tasks routinely performed by competent physicians.

Accordingly, it is the Applicants' position that the specification clearly teaches methods bearing good correlation to the entire scope of all the claims, indicating that the test of enablement has been met.

In view of the foregoing, it is respectfully submitted that the rejections under 35 U.S.C. § 112 do not apply. Withdrawal of the rejections and reconsideration are respectfully requested.

Claim Rejections - 35 U.S.C. § 103(a)

Claims 1, 5-12, 14, 15, and 22-52 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Cheng I or Cheng II (see, items 9 and 11 on pages 9 and 11 of the Office Action). In addition, claims 16-21 and 53-58 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Cheng I or Cheng II in view of U.S. Patent No. 6,120,751 to Unger ("Unger") (item 13 on page 13 of the Office Action). The rejections are respectfully traversed.

Neither Cheng reference discloses, teaches or suggests the treatment of particular diseases and disorders recited in claim 1. The Examiner has repeated his previously raised point that retinitis can be characterized as one of the conditions of eye trauma. The entire disagreement is now whether retinitis can or cannot be characterized as one of the conditions of eye trauma. The Examiner insists it can be, and the Applicants continue to respectfully disagree.

In support of their position, the Applicants provide a Declaration under Rule 132 from Dr. William R. Freeman. As stated in the Declaration, retinitis is a disease characterized by the inflammation of the retina, e.g., caused by cytomegalovirus infection or by other infection. The term "retinitis" does not include "trauma," which is how those skilled in the art refer to a mechanical injury to an eye cause by some kind of blow or impact. The Declaration, therefore, clearly establishes that it would not be proper to extend the treatments used for retinitis to be used to treat traumas. Also, please note that the claims have been amended and inflammation is no longer recited, thus even more clearly distinguishing the present claims from the cited references (the Examiner stated that inflammation is related to retinitis).

The Applicants submit that the Examiner's rationale does not provide a good reason for making a *prima facie* case of obviousness. Such a notion has no support in medical literature anywhere and there is no known treatment of eye traumas using any kind of retinitis medication.

Unger fails to eliminate the above discussed deficiencies of Cheng I or II. Unger only teaches compositions for targeted drug delivery and has not a word discussing or even remotely suggesting any eye treatments. There is nothing in Unger regarding the use of such compositions for the treatment of the above-mentioned ocular diseases and disorders.

It is, therefore, submitted that there is no evidence suggesting that a skilled artisan knowing the teachings of Cheng I and II and Unger, would without more, be motivated to make a modification described by the Examiner by combining Cheng I and/or II with Unger.

In view of the foregoing, it is respectfully submitted claim 1 is patentably distinguishable over Cheng I and II in view of Unger. Each of other claims depends, directly or indirectly, on claim 1, and is allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

The Commissioner is hereby authorized to charge $65.00 as payment for the Petition for the One-Month Extension of Time fee to Deposit Account No. 07-1896. No other fee is believed due in connection with the filing of this paper. However, the Commissioner is hereby authorized to charge any other fees that may be due in connection with the filing of this paper, or credit any overpayment to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

Date: April 23, 2009

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